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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/849,597	05/07/2001	Han Oh Park	3275-0108P	8892

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EXAMINER	
CHUNDURU, SURYAPRABHA	
ART UNIT	**PAPER NUMBER**
1637	

DATE MAILED: 10/17/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/849,597	PARK ET AL.	
	Examiner	Art Unit	
	Suryaprabha Chunduru	1637	

-- Th MAILING DATE of this communication app ars on the cover she t with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on 8/18/03 .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-3 and 5-14 is/are pending in the application.

4a) Of the above claim(s) 2 is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1,3 and 5-14 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. Upon reconsideration of request for withdrawal of improper finality, the finality of the previous office action is withdrawn herein.

2. Applicants' response to the office action (Paper No. 20) filed on June 2, 2003 has been entered and considered. Claims 1, 3, 5-14 are pending in this application and are reconsidered for examination.

Response to arguments

3. Applicants' response to the office action (Paper No. 20) is fully considered and found persuasive.

4. With reference to the rejection made under 35 USC 102(b), Applicant's arguments have been fully considered and the rejection is withdrawn in view of the arguments (Paper No. 20).

5. With reference to the rejection made under 35 USC 103(a), Applicant's arguments have been fully considered and the rejection is withdrawn in view of the arguments (Paper No. 20).

Claim Rejections - 35 USC § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out

the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

A. Claims 1, 3, 5-9, 12-14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Padegimas et al. (Analytical Biochem., Vol. 260, pages 149-153,1998) and in view of Deugau et al. (USPN. 5,858,656).

Padegimas et al. teach a process of claims 1 and 3, for preparing a library of DNA fragments of which terminal sequences are known by using a DNA of which base sequence is completely unidentified, wherein Padegimas et al. disclose that the method comprises (i) digesting a DNA into fragments which have the single-stranded cohesive ends by using a restriction enzyme (see page 150, column 1, paragraph 2); (ii) preparing hairpin loop adapters which have single-strand cohesive ends (see page 150, column 1, paragraph 3, page 151, column 1, paragraph 1); (iii) ligating the DNA fragments with the hairpin loop adapter by using DNA ligase (see page 150, column 1, paragraph 4); (iv-vi) removing unligated DNA fragments and hairpin loop adapters and eliminating hairpin loop structure from DNA fragments, by using exonuclease (see page 150, column 1, paragraph 4, column 2, lines 1-4) and amplifying the DNA fragments by using a DNA polymerase and a primer which can combine complimentarily to a residual sequence from the adapter (see page 150, column 2, paragraph 1, page 151 Figs. 1 and 2).

With regard to claims 7, Padegimas et al. also teach that the method comprises (i) ligase as T4 DNA ligase (see page 150, column 1, paragraph 4);

With regard to claim 8, Padegimas et al. teach that the exonuclease of step (iv) as exonulcease III (see page 150, column 1, paragraph 4, column 2, lines 1-4);

However, Padegimas et al did not teach step (v) eliminating a hairpin loop structure from DNA fragments which contain the hairpin loop adapters, by using an alkaline solution or an RNase or a single-strand specific exonuclease and use of type IIS or IP type restriction endonucleases.

Deugau et al. teach a method of claims 1, and 2, for adaptor mediated preparation of a target DNA fragment comprising (i) digesting or cleaving DNA with type IIS or IP type (interrupted palindrome recognizing restriction endonuclease) restriction endonucleases (see column 7, lines 32-67, column 8, lines 1-10);

With regard to claims, 1 and 9, Deugau et al. teach removal of unligated adaptors by a simple washing procedure or by denaturation process (see column 10, lines 47-58) followed by resuspending in buffer containing alkaline solution (buffer D) (see column 17, lines 24-26);

With regard to claim 12, use of taq DNA polymerase in PCR reaction (see column 18, lines 31-40).

With regard to Claims 13-14, Deugau et al. teach that the hairpin loop adapters have single-strand cohesive ends comprising all sorts of single-stranded DNA obtained by a random combination of four nucleotides (see column 9, lines 12-37).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to combine the method for preparing a library of DNA fragments as taught by Padegimas et al. with the teachings as taught by Deugau et al., which is applicable to eliminate hairpin loop structures because Deugau et al. suggests that 'removal of the non-ligated

fragments requires only a simple washing procedure or alternately, denaturation process to isolate linker-DNA fragment complex, which can be used as a template in sequencing procedure or for preparation of hybridization probes.(see column 10, lines 53-65)." An ordinary practitioner would have been motivated to combine the method of preparing a library of DNA fragments by adaptor ligation based PCR as taught by Padegimas et al. with teachings as taught by Deugau et al. by incorporating the limitations as removal of hairpin loop structures from the ligated DNA fragments, which would reduce, background noise and aid in quick isolation of selective ligated products thereby enhancing selective amplification DNA fragments with increased sensitivity and specificity.

B. Claims 10-11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Padegimas et al. (Analytical Biochem., Vol. 260, pages 149-153,1998) and in view Backman et al. (USPN. 5,516,663).

Padegimas et al. teach a process of claims 1 and 3, for preparing a library of DNA fragments of which terminal sequences are known by using a DNA of which base sequence is completely unidentified, wherein Padegimas et al. disclose that the method comprises (i) digesting a DNA into fragments which have the single-stranded cohesive ends by using a restriction enzyme (see page 150, column 1, paragraph 2); (ii) preparing hairpin loop adapters which have single-strand cohesive ends (see page 150, column 1, paragraph 3, page 151, column 1, paragraph 1); (iii) ligating the DNA fragments with the hairpin loop adapter by using DNA ligase (see page 150, column 1, paragraph 4); (iv-vi) removing unligated DNA fragments and hairpin loop adapters and eliminating hairpin loop structure from DNA fragments, by using exonuclease (see page 150, column 1, paragraph 4, column 2, lines 1-4) and amplifying the DNA

fragments by using a DNA polymerase and a primer which can combine complimentarily to a residual sequence from the adapter (see page 150, column 2, paragraph 1, page 151 Figs. 1 and 2).

However, Padegimas et al did not teach step (v) eliminating a hairpin loop structure from DNA fragments which contain the hairpin loop adapters, by using an alkaline solution or an RNase or a single-strand specific exonuclease.

With regard to claims 1, and 9-11, Backman et al. teach a method amplifying a target nucleic acid wherein Backman et al. teach that the method comprises eliminating abasic residue or over hang (hairpin loop structure) by cleaving the ligated DNA fragments by using RNAse or alkali (see column 4, lines 15-35) or endonuclease IV, which acts as a single-strand specific exonuclease (see column 9, lines 1-27, column 10, column 11, lines 40-67, column 12, lines 1-2).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to combine the method as taught by Padegimas et al. with the correction of ligated products as taught by Backman et al., which is applicable to eliminate hairpin loop structures because Backman suggests that 'to avoid problems of contamination, the ligated products are cleaved using various RNases or alkaline conditions before amplification (see column 10, lines 14-21). An ordinary practitioner would have been motivated to combine the method of generating a library of DNA fragments as taught by Padegimas et al. with the use of mechanism for controlling contamination as taught by Backman et al. by limiting the ligated DNA fragments free of hairpin loop structures, for the advantages of reducing background noise and contamination during PCR amplification and for the benefit of developing a method of amplification with increased sensitivity and specificity.

Conclusion

No claims are allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Suryaprabha Chunduru whose telephone number is 703-305-1004. The examiner can normally be reached on 8.30A.M. - 4.30P.M, Mon - Friday.

If attempts to reach the examiner are unsuccessful, the primary examiner in charge of the prosecution of this case, Jeffrey Fredman can be reached at 703-308-6568. If attempts to reach the examiners by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 703-308-1119. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3014 for regular communications and - for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Suryaprabha Chunduru
October 9, 2003

JEFFREY FREDMAN
PRIMARY EXAMINER